

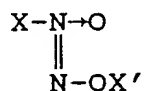
We claim:

1. A polymeric composition capable of releasing nitric oxide under physiological conditions, said composition comprising a biopolymer and a nitric oxide-releasing  $\text{N}_2\text{O}_2^-$  functional group bound to said biopolymer.

2. The polymeric composition of claim 1, wherein said biopolymer is selected from the group consisting of a peptide, polypeptide, protein, oligonucleotide, and nucleic acid.

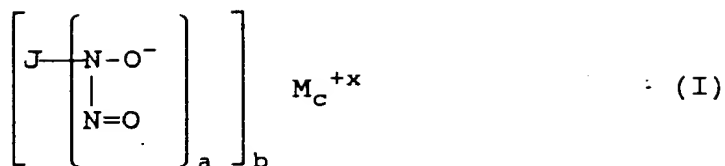
3. The polymeric composition of claim 2, wherein said biopolymer is selected from the group consisting of a tissue-, cell-, or tumor-specific antibody or fragment thereof, a protein containing a recognition sequence for a receptor-ligand interaction favorable to tumor cell attachment, an anti-chemotactic agent, and a hormone.

4. The polymeric composition of claim 1, wherein said nitric oxide-releasing  $\text{N}_2\text{O}_2^-$  group is of the formula



wherein X is an organic or inorganic moiety and X' is selected from the group consisting of X, a pharmaceutically acceptable metal center or a pharmaceutically acceptable cation, and wherein said  $\text{N}_2\text{O}_2^-$  group is bonded to said biopolymer through at least one of X or X'.

5. The polymeric composition of claim 4, wherein said nitric oxide-releasing  $\text{N}_2\text{O}_2^-$  functional group is of the formula:

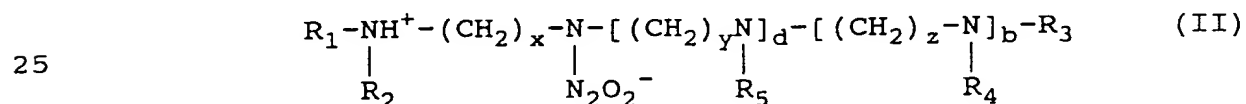


5 wherein J is an organic or inorganic moiety,  $\text{M}^{+x}$  is a pharmaceutically acceptable cation, where x is the valence of the cation, a an integer of at least one, and b and c are the smallest integers that result in a neutral compound.

15 6. The method of claim 5, wherein J is a moiety which is linked to the nitrogen of the remainder of the complex through an atom other than a carbon atom.

7. The polymeric composition of claim 5, wherein the nitric-oxide releasing group is a compound other than a salt of alanosine or dopastin.

20 8. The polymeric composition of claim 4, wherein said nitric oxide-releasing  $\text{N}_2\text{O}_2^-$  functional group is of the formula:

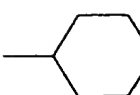
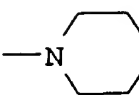


30 wherein b and d are the same or different and may be zero or one,  $\text{R}_1$ ,  $\text{R}_2$ ,  $\text{R}_3$ ,  $\text{R}_4$ , and  $\text{R}_5$  are the same or different and may be hydrogen,  $\text{C}_{3-8}$  cycloalkyl,  $\text{C}_{1-12}$  straight or branched chain alkyl, benzyl, benzoyl, phthaloyl, acetyl, trifluoroacetyl, p-toluyyl, t-butoxycarbonyl, or 2,2,2-trichloro-t-butoxycarbonyl, and x, y, and z are the same or different and are integers from 2 to 12.

40 9. The polymeric composition of claim 4, wherein said nitric oxide-releasing  $\text{N}_2\text{O}_2^-$  functional group is of the formula:

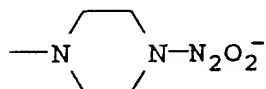


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wherein B is  or  , R<sub>6</sub>

and R<sub>7</sub> are the same or different and may be hydrogen,  
 10 C<sub>3-8</sub> cycloalkyl, C<sub>1-12</sub> straight or branched chain alkyl,  
 benzyl, benzoyl, phthaloyl, acetyl, trifluoroacetyl, p-  
 toluyyl, t-butoxycarbonyl, or 2,2,2-trichloro-t-  
 butoxycarbonyl, f is an integer from 0 to 12, with the  
 proviso that when B is the substituted piperazine moiety

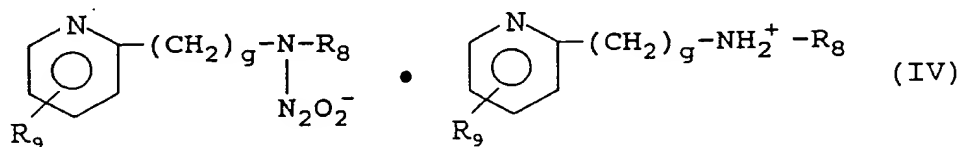
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then f is an integer from 2 to 12.

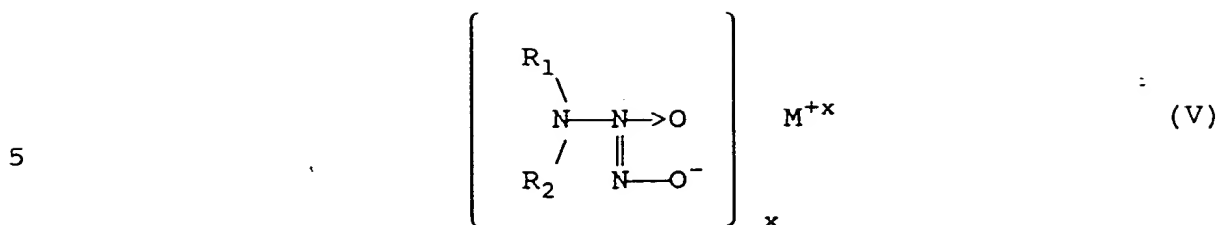
10. The polymeric composition of claim 4, wherein  
 20 said nitric oxide-releasing N<sub>2</sub>O<sub>2</sub><sup>-</sup> functional group is of  
 the formula:

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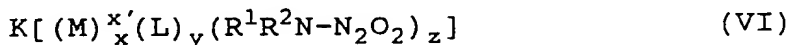
wherein R<sub>8</sub> is hydrogen, C<sub>3-8</sub> cycloalkyl, C<sub>1-12</sub> straight or  
 branched chain alkyl, benzyl, benzoyl, phthaloyl,  
 30 acetyl, trifluoroacetyl, p-toluyyl, t-butoxycarbonyl, or  
 2,2,2-tri-chloro-t-butoxycarbonyl, R<sub>9</sub> is hydrogen or a  
 C<sub>1</sub>-C<sub>12</sub> straight or branched chain alkyl, and g is 2 to 6.

11. The polymeric composition of claim 4, wherein  
 35 said nitric oxide-releasing N<sub>2</sub>O<sub>2</sub><sup>-</sup> functional group is of  
 the formula:



wherein  $R_1$  and  $R_2$  are independently selected from the group consisting of a straight chain or branched chain  $C_1 - C_{12}$  alkyl group and a benzyl group, or else  $R_1$  and  $R_2$  together with the nitrogen atom they are bonded to form a heterocyclic group, a pyrrolidino, piperidino, piperazino or morpholino group,  $M^{+x}$  is a pharmaceutically acceptable cation, and  $x$  is the valence of the cation.

12. The polymeric composition of claim 4, wherein said nitric oxide-releasing  $N_2O_2^-$  functional group is of the formula:



wherein  $M$  is a pharmaceutically acceptable metal, or, where  $x$  is at least two, a mixture of two different pharmaceutically acceptable metals,  $L$  is a ligand different from  $(R^1R^2N-N_2O_2)$  and is bound to at least one metal,  $R^1$  and  $R^2$  are each organic moieties and may be the same or different,  $x$  is an integer of from 1 to 10,  $x'$  is the formal oxidation state of the metal  $M$ , and is an integer of from 1 to 6,  $y$  is an integer of from 1 to 18, and where  $y$  is at least 2, the ligands  $L$  may be the same or different,  $z$  is an integer of from 1 to 20, and  $K$  is a pharmaceutically acceptable counterion to render the compound neutral to the extent necessary.

13. The polymeric composition of claim 4, wherein said nitric oxide-releasing  $N_2O_2^-$  functional group is of the formula:



wherein R is C<sub>2-8</sub> lower alkyl, phenyl, benzyl, or C<sub>3-8</sub> cycloalkyl, any of which R groups may be substituted by one to three substituents, which are the same or  
 5 different, selected from the group consisting of halo, hydroxy, C<sub>1-8</sub> alkoxy, -NH<sub>2</sub>, -C(O)NH<sub>2</sub>, -CH(O), -C(O)OH, and -NO<sub>2</sub>, X is a pharmaceutically acceptable cation, a pharmaceutically acceptable metal center, or a  
 10 pharmaceutically acceptable organic group selected from the group consisting of C<sub>1-8</sub> lower alkyl, -C(O)CH<sub>3</sub>, and -C(O)NH<sub>2</sub>, and y is one to three, consistent with the valence of X.

14. The polymeric composition of claim 4, wherein  
 15 said nitric oxide-releasing N<sub>2</sub>O<sub>2</sub><sup>-</sup> functional group is of the formula:



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wherein R<sub>1</sub> and R<sub>2</sub> are independently chosen from C<sub>1-12</sub> straight chain alkyl, C<sub>1-12</sub> alkoxy or acyloxy substituted straight chain alkyl, C<sub>2-12</sub> hydroxy or halo substituted  
 25 straight chain alkyl, C<sub>3-12</sub> branched chain alkyl, C<sub>3-12</sub> hydroxy, halo, alkoxy, or acyloxy substituted branched chain alkyl, C<sub>3-12</sub> straight chain olefinic and C<sub>3-12</sub> branched chain olefinic which are unsubstituted or substituted with hydroxy, alkoxy, acyloxy, halo or  
 30 benzyl, or R<sub>1</sub> and R<sub>2</sub> together with the nitrogen atom to which they are bonded form a heterocyclic group, a pyrrolidino, piperidino, piperazino or morpholino group, and R<sub>3</sub> is a group selected from C<sub>1-12</sub> straight chain and C<sub>3-12</sub> branched chain alkyl which are unsubstituted or  
 35 substituted by hydroxy, halo, acyloxy or alkoxy, C<sub>2-12</sub> straight chain or C<sub>3-12</sub> branched chain olefinic which are unsubstituted or substituted by halo, alkoxy, acyloxy or hydroxy, C<sub>1-12</sub> unsubstituted or substituted acyl, sulfonyl and carboxamido; or R<sub>3</sub> is a group of the

formula  $-(CH_2)_n-ON=N(O)NR_1R_2$ , wherein  $n$  is an integer of 2-8, and  $R_1$  and  $R_2$  are as defined above; with the proviso that  $R_1$ ,  $R_2$  and  $R_3$  do not contain a halo or a hydroxy substituent  $\alpha$  to a heteroatom.

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15. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and the polymeric composition of claim 1.

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16. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and the polymeric composition of claim 2.

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17. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and the polymeric composition of claim 3.

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18. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and the polymeric composition of claim 4.

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19. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and the polymeric composition of claim 5.

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20. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and the polymeric composition of claim 6.

21. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and the polymeric composition of claim 7.

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22. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and the polymeric composition of claim 8.

23. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and the polymeric composition of claim 9.

5           24. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and the polymeric composition of claim 10.

10           25. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and the polymeric composition of claim 11.

15           26. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and the polymeric composition of claim 12.

20           27. A method of treating a biological disorder in a mammal in which dosage with nitric oxide is therapeutic, comprising administering to said mammal the polymeric composition of claim 1 in an amount sufficient to release a therapeutically effective amount of nitric oxide.

25           28. A method of treating a biological disorder in a mammal in which dosage with nitric oxide is therapeutic, comprising administering the polymeric composition of claim 2 in an amount sufficient to release a therapeutically effective amount of nitric oxide.

30           29. A method of treating a biological disorder in a mammal in which dosage with nitric oxide is therapeutic, comprising administering the polymeric composition of claim 3 in an amount sufficient to  
35           release a therapeutically effective amount of nitric oxide.

30. A method of treating a biological disorder in a mammal in which dosage with nitric oxide is therapeutic, comprising administering the polymeric composition of claim 4 in an amount sufficient to  
5 release a therapeutically effective amount of nitric oxide.

31. A method of treating a biological disorder in a mammal in which dosage with nitric oxide is  
10 therapeutic, comprising administering the polymeric composition of claim 5 in an amount sufficient to release a therapeutically effective amount of nitric oxide.

32. A method of treating a biological disorder in a mammal in which dosage with nitric oxide is  
15 therapeutic, comprising administering the polymeric composition of claim 6 in an amount sufficient to release a therapeutically effective amount of nitric  
20 oxide.

33. A method of treating a biological disorder in a mammal in which dosage with nitric oxide is  
25 therapeutic, comprising administering the polymeric composition of claim 7 in an amount sufficient to release a therapeutically effective amount of nitric oxide.

34. A method of treating a biological disorder in  
30 a mammal in which dosage with nitric oxide is therapeutic, comprising administering the polymeric composition of claim 8 in an amount sufficient to release a therapeutically effective amount of nitric  
oxide.

35. A method of treating a biological disorder in  
a mammal in which dosage with nitric oxide is



therapeutic, comprising administering the polymeric composition of claim 9 in an amount sufficient to release a therapeutically effective amount of nitric oxide.

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36. A method of treating a biological disorder in a mammal in which dosage with nitric oxide is therapeutic, comprising administering the polymeric composition of claim 10 in an amount sufficient to release a therapeutically effective amount of nitric oxide.

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37. A method of treating a biological disorder in a mammal in which dosage with nitric oxide is therapeutic, comprising administering the polymeric composition of claim 11 in an amount sufficient to release a therapeutically effective amount of nitric oxide.

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38. A method of treating a biological disorder in a mammal in which dosage with nitric oxide is therapeutic, comprising administering the polymeric composition of claim 12 in an amount sufficient to release a therapeutically effective amount of nitric oxide.

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